REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks are respectfully requested. Claims 1-6 and 21-29 are currently pending in the application. Claims 1-6 were cancelled because these claims were withdrawn from consideration as being drawn to a non-elected invention, and not for any reasons related to patentability. Accordingly, claims 21-29 are at issue.

The applicants have amended claim 21 to be directed to an isolated polypeptide fragment of *Clostridium sordellii* lethal toxin (LT) with glucosyltransferase activity, consisting of approximately the first 1020 N-terminal amino acids of the amino acid sequence of *Clostridium sordellii* lethal Toxin (LT) according to SEQ ID NO: 6. Support for amended claim 21 can be found throughout the specification, for example, on page 5, lines 18 and 19; page 7, lines 22-25; page 10, lines 6-9, and 14-17; page 12, lines 13-19; and page 23, lines 32 and 33.

The applicants have amended claim 22 to be directed to a compound consisting of a polypeptide fragment of *Clostridium sordellii* lethal Toxin (LT) consisting of approximately the first 1020 amino acids of the amino acid sequence of *Clostridium sordellii* lethal Toxin (LT) according to SEQ ID NO: 1, or a portion thereof, the compound having (i) a glucosyltransferase activity domain, and (ii) a target cell specific binding domain which permits the compound to bind to a target cell. Support for amended claim 22 can be found throughout the specification, for example, on page 10, lines 16-18, page 10, lines 27 to page 11, line 19 and page 23, lines 19-32.

The applicants have amended claim 23 to be directed to a compound consisting of a polypeptide fragment of *Clostridium sordellii* lethal Toxin (LT) consisting of approximately the first 1020 amino acids of the amino acid sequence of *Clostridium sordellii* lethal Toxin (LT) as defined by SEQ ID NO: 1, or a portion thereof, the compound having (i) a glucosyltransferase activity domain, (ii) a target cell specific binding domain, which domain causes the compound to bind to a target cell, and (iii) a translocation domain causes the compound to bind to a target cell, and (iv) a translocation domain for translocating a catalytic domain of *Clostridium sordellii* lethal Toxin (LT) from the exterior of a cell into the interior of said cell. Support for amended claim 23 can be found throughout the specification, for example, on page 7, lines 28-36.

The applicants have amended claim 26 to be directed to a compound consisting of a compound according to one of claims 22 to 24 and a pharmaceutically acceptable adjuvant or carrier. Support for amended claim 26 can be found throughout the specification, for example, on page 5, lines 1-13.

Claim 27 has been amended to be directed to a composition consisting of a compound according to claim 25 and a pharmaceutically acceptable adjuvant or carrier. Support for amended claim 27 can be found throughout the specification, for example, on page 5, lines 1-15.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Patentability Remarks

The Rejection Under 35 U.S.C. § 112, first paragraph, Should Be Withdrawn

On pages 2 and 3 of the official action, the examiner rejected claims 21, 22 and claimed dependents therefrom under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description. With regard to claim 21, the examiner alleged that although the specification teaches that a further object of the invention is a "vector" containing a nucleotide acid fragment which codes for the first 1020 amino acids of toxin LT or parts thereof, the claims read on a polypeptide fragment for which there is no clear support in the specification.

With regard to claim 22, the examiner alleged that claim 22 comprises two parts, a polypeptide fragment consisting of the first 1020 amino acids of SEQ ID NO: 1, and a target cell specific binding domain, which permits the compound to bind to a target cell. The examiner asserted however, the specification only contemplates an "immunotoxin" comprising three parts: a target cell binding domain, a translocation domain, and a catalytic domain of the LT toxin. The examiner further alleged these three parts of the immunotoxin are connected by covalent bonds. The applicants respectfully traverse the rejection.

In order for the applicant to meet the §112, written description requirement, one need not "describe exactly the subject matter claimed, [instead] the description must clear allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *See Enzo Biochem.*, 52 U.S.P.Q.2d at 1135-1136 (citing *In re Wands*, 858 F.2d. 731, 737 (Fed

Cir. 1988)); *see also Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991)).

Claim 21 is supported by the combination of the following teachings in the specification. On page 10, lines 6-9, as discussed in the official action, the specification teaches a vector containing a nucleotide fragment which codes for the first 1020 amino acids of toxin LT or parts thereof having the toxic activity of the catalytic domain. On page 12, lines 13-19, the specification teaches expression of this type of vector to generate a polypeptide consisting of the aminoterminal 1020 amino acids or a fragment thereof with the preserved glucosyltransferase activity. The specification further teaches the glucosyltransferase activity is toxic and associated with the catalytic domain of LT (see page page 10, lines 8, 9, 14, and 15). These teachings from the specification convey with reasonable clarity to those skilled in the art that the inventor was in possession of an isolated polypeptide fragment of *Clostridium sordelli* lethal Toxin (LT) with glucosyltransferase activity, consisting of approximately the first 1020 N-terminal amino acids of the *Clostridium sordelli* lethal Toxin (LT). It would absolutely defy logic to conclude otherwise.

With regard to claim 22, the specification teaches on page 10, lines 27 to page 11, line 19 several different compounds consisting of a toxin and a target cell binding domain. Specifically, the specification teaches a toxin can be either chemically coupled, expressed through molecule recombinant techniques, or fused to binding domains such as the VH or VL antibody domains, which can recognize specific targets. Dipththeria toxin, Pseudomonas exotoxin A and LT of *C. sordelli* are examples of the catalytic domains within the bacterial toxins used for constructing this type of immunotoxin (see page 23, lines 19-32). LT of *C. sordelli* is the preferred toxin (see page 10, lines 16-18). Again, these teaching from the specification convey with reasonable clarity to those skilled in the art that the inventor was in possession of the claimed compound of claim 23. Accordingly, the applicants request that the rejections under 35 U.S.C. §112, first paragraph, (written description) be withdrawn.

The Rejection Under 35 U.S.C. §§102 (a) and (b) Should Be Withdrawn

On pages 3 and 4 of the official action, the examiner rejected claims 22-24, 26, 28, and 29 under 35 U.S.C. § 102(b) as being anticipated by Popoff, *Infection and Immunity* 55:35-43 (1987) (hereafter Popoff). Specifically, the examiner has maintained the rejection because the claims are not directed to a specific fragment, rather the claims encompass a compound (interpreted as a compound) "comprising" a polypeptide fragment of *Clostridium*

sordelli lethal Toxin consisting of the first 1020 amino acids of the amino acid sequence of *Clostridium sordelli* lethal Toxin according to SEQ ID NO: 6 and/or a target cell specific binding domain which permits the compound to bind to a target cell and/or a translocation domain for translocating a catalytic domain of *Clostridium sordelli* lethal Toxin (LT) from the exterior of the cell into the interior of the cell, which the examiner alleged is inherently taught by Popoff. The examiner also asserted that the polypeptide of Popoff inherently comprises the claimed fragments and domains of the claimed invention.

In addition, the examiner rejected claims 22-24 under 35 U.S.C. § 102(a) as being anticipated by Green *et al., Gene* 161:57-61 (1995) (hereafter Green). Specifically, the examiner alleged the specification notes that the DNA and protein sequence of toxin LT as described by Green anticipates the complete amino acid sequence or polypeptide of the toxin LT. The examiner further alleged Green anticipates the claimed compound because the known polypeptide encompasses a compound "comprising" a polypeptide fragment of *Clostridium sordelli* lethal Toxin consisting essentially of approximately the first 1020 amino acids of the amino acid sequence of *Clostridium sordelli* lethal Toxin according to SEQ ID NO: 6 and/or a target cell specific binding domain and or a translocation domain consisting essentially of approximately the N-terminal amino acids 1021-1700 of the amino acid sequence of *Clostridium sordelli* lethal Toxin (LT). In view of the foregoing claim amendments, the applicants respectfully traverse the rejection.

In view of the foregoing amendment to the claims, the rejection under 35 U.S.C. § 102(b) over Popoff and 35 U.S.C. § 102(a) Green is now moot. Solely for purposes of expediting prosecution and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have amended claims 22-24 and 26 to distinguish the claimed invention over the cited document. The amended claims is directed to a polypeptide consisting of the first 1020 amino acids of the amino acid sequence of *Clostridium sordelli* lethal Toxin according to SEQ ID NO: 6 and/or a target cell specific binding domain and/or a translocation domain which are neither disclosed nor suggested by the cited document. In view of the foregoing, the applicants submit that neither cited document anticipates the presently claimed invention. Therefore, the applicants respectfully request that the rejection under §§ 102(a) and (b) be withdrawn.

The Rejection under 35 U.S.C. §103(a) Should Be Withdrawn

On pages 6 and 7 of the official action, the examiner maintained the rejection of claims 21-29 under 35 U.S.C. § 103(a) as being unpatentable over Popofff in combination with the teaching of Blakey *et al.* Essentially, the examiner alleged that although the Popoff reference does not characterize the domains of the lethal toxin, the reference does teach the isolation of LT and a pharmaceutical composition comprising LT. Thus, the examiner concluded Popoff is obvious in view of Blakey since the LT polypeptide inherently "comprises" the specifically claimed fragments and domains. The applicants respectfully traverse the rejection.

This rejection has been rendered moot by the foregoing amendment of the relevant claims. Claims 21-29 are now directed to a compound **consisting of** a polypeptide fragment of *Clostridium sordellii* lethal Toxin (LT) consisting essentially approximately the first 1020 amino acids of the amino acid sequence of *Clostridium sordellii* lethal Toxin (LT) according to SEQ ID NO: 6 or SEQ ID NO: 1, and/or the compound having (i) a glucosyltransferase activity domain, and (ii) a target cell specific binding domain permitting the compound to bind to a target cell and/or (iii) a translocation domain causing the compound to bind to a target cell, and (iv) a translocation domain for translocating a catalytic domain of *Clostridium sordellii* lethal Toxin (LT) from the exterior of a cell line into the interior of said cell wherein the target cell specific binding domain can be an antibody and the compound is in a pharmaceutically acceptable adjuvant. Popoff neither teaches nor suggests the claimed compound *consisting of* the fragments and domains as claimed. Further, one of skill in the art would not be motivated to generate the claimed compound as claimed because (1) the domains of the lethal toxin are not defined in Popoff and (2) Popoff does not teach or suggest the use of other binding and translocation domains (see specification at page 10).

Blakey *et al.* is cited in this rejection only for its teachings related coupling antibodies to toxins. Since Popoff is silent with regard to coupling antibodies to toxins and fails to teach the various domains (binding, catalytic, and translocation) of the LT protein, there would have been no motivation to combine Popoff with Blakey.

Accordingly, Popoff, either alone or in combination with Blakey, neither disclose nor suggest the claimed compound and compositions of claims 21-29. Therefore, the applicants respectfully request the withdrawal of the rejection based on 35 U.S.C. § 103 (a).

CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, the examiner is strongly urged to contact the undersigned at the telephone number listed below.

Respectfully submitted,

PILLSBURY WINTHROP LLP

By: _____

Thomas A. Cawley, Jr., Ph.D.
Reg. No.: 40,944
Tel. No.: (703) 905-2144
Fax No.: (703) 905-2500

TAC\PAJ
PO Box 10500
McLean, VA 22102
(703) 905-2000